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(54) **A method for the preparation of a sterile dialysis fluid for medical use or a similar physiologically acceptable sterile fluid.**

(57) A method for the preparation of a sterile dialysis fluid for medical use or a similar physiologically acceptable sterile fluid by which method water is continuously transported from a source (A) for the same to a point of consumption (G), necessary concentrates in liquid and/or powder form being added during the transport.

The method according to the invention is characterized in that the water with or without concentrate is heated during the transport to sterilization temperature and is kept at this temperature during the time required for the sterilization, whereafter it is cooled to the desired consuming temperature.

The invention also relates to a system for the preparation of a sterile dialysis fluid or a similar physiologically acceptable fluid by means of the above method, comprising a pipeline between the said source for the water (A) and the point of consumption (G), e g a draw-off point, this pipeline comprising means (8,8') for the pumping of water, means (3) for its heating, means (2,6) for its cooling and means (eg 21 and 23) for the supply of necessary concentrates in liquid and/or powder form.

The system according to the invention is characterized in that the pipeline between the said means (3 and 2,6) for heating and cooling respectively of water is dimensioned so in relation to the capacity of the said means (8,8' and 3) for pumping and heating respectively that the sojourn time of the water within this part X-Y of the pipeline will be sufficient for the sterilization.

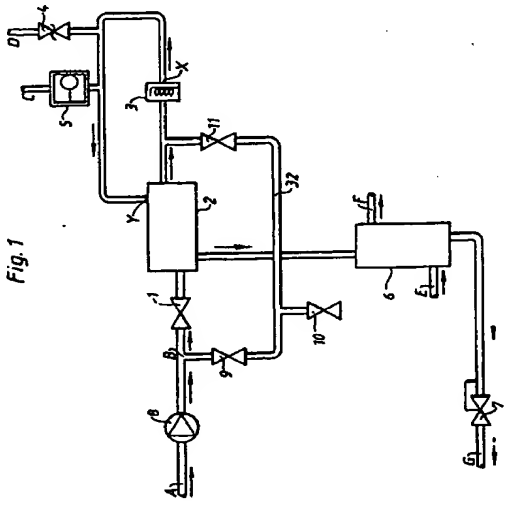

Fig.1

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A METHOD FOR THE PREPARATION OF A STERILE DIALYSIS FLUID FOR MEDICAL USE OR A SIMILAR PHYSIOLOGICALLY ACCEPTABLE STERILE FLUID

TECHNICAL FIELD

The present invention relates to a method for the preparation of a sterile dialysis fluid for medical use or a similar physiologically acceptable sterile fluid by which method water is continuously transported from a source for the same to a point of consumption, necessary concentrates in liquid and/or powder form being added during the transport.

The invention also relates to a system for the preparation of a sterile dialysis fluid or a similar physiologically acceptable fluid by means of the above method, comprising a pipeline between said source for the water and the point of consumption, e g a draw-off point, this pipeline comprising means for the pumping of water, means for its heating, means for its cooling and means for the supply of necessary concentrates in liquid and/or powder form.

The invention is this intended primarily to be employed in connection with preparation of a dialysis fluid, but can also be used for the preparation of other sterile fluids, e g wound cleansing fluid.

BACKGROUND ART

The manufacture of sterile solutions and infusion solutions is regulated in national and international legislation with regard to the demands to be made in respect of chemical and microbiological purity. The method of sterilization generally used is steam autoclaving, that is to say sterilization with saturated water vapour at high temperature. A customary choice of parameters is 121 °C for 15 minutes.

The fluid which is sterilized may be e g a physiological salt solution packed in some kind of container which usually consists of plastics or glass.

The disadvantage of the above mentioned system is obvious. As the refining value is low, the cost of handling and transport signify a great deal for the final cost of the product.

The present invention is based on the principle of producing the sterile solution directly at the place of application. The field of application here is very wide. It may be a matter of solutions which are used in dialysis, e g sterile CAPD solution or sterile hemofiltration solution or dialysis solution for conventional hemodialysis. Other fields of application are e g sterile wound cleansing solutions and sterile infusion solutions of different types. The above mentioned solutions may be produced in that water of suitable chemical and microbiological quality is prepared and is sterilized subsequently as the type of consumption necessitates. In accordance with the invention it is intended for this to take place continuously in a pipe system at the location of the actual utilization.

To check the resulting sterilization spores of Bacillus stearothermophilus bacteria may be used which, owing to their resistance, are a generally accepted indicator organism in steam sterilization.

The D-value is defined as the time it take to kill a ^{10}logarithm of a given quantity of the spore form of Bacillus stearothermophilus at a given temperature. The lowest accepted D-value at 120 °C for Bacillus stearothermophilus is 1.5 minutes. If the temperature is raised by 10 °C the D-value generally drops to one tenth. This means that 130 °C furnishes a D-value of the order of magnitude of 0.15 minutes.

The concept "sterile" implies free from living microorganisms. This requirement is converted in practice to a statistic definition. This means that on 1 000 000 units produced there may be not more than 1 unit with 1 surviving microorganism. This final result can be achieved by two methods, on the one hand by the overkilling concept, which implies that the sojourn time during sterilization should correspond to the killing of 12 D-values (10^{12} spores of Bacillus stearothermophilus) or a concept which is based on the true number of heat-resistant microorganisms which are present in the solution prior to the sterilization. This concept makes it necessary, therefor, for the said number to be known. At the same time it normally means that a smaller number of D-values can be used. In general it is customary for the sojourn time to be adjusted to 8-10 D-values.

DISCLOSURE OF INVENTION

By the present invention a method is thus established for the preparation of a sterile dialysis fluid for medical use or a similar physiologically acceptable sterile fluid by which method water is continuously transported from a source for the same to a point of consumption, necessary concentrates in liquid and/or powder form being added during the transport.

The method according to the invention is characterized in that the water with or without concentrate is treated during the transport to sterilizing

temperature and is kept at this temperature during the time required for the sterilization, whereafter it is cooled to the desired consuming temperature.

The invention also relates to a system for the preparation of a sterile dialysis fluid or a similar physiologically acceptable fluid by means of the above defined method, comprising a pipeline between the said source for the water and the point of consumption, e g a draw-off point, this pipeline comprising means for the pumping of the water, means for its heating, means for its cooling and means for the supply of necessary concentrates in liquid and/or powder form.

This system is characterized in that the pipeline between the said means for heating and cooling respectively of the water is dimensioned so in relation to the capacity of said means for pumping and heating respectively that the sojourn time of the water within this part of the pipeline will be sufficient for the sterilization.

The said means for cooling preferably comprises a heat exchanger for a first cooling of the water with the help of the incoming, not yet heated, water. In this way good heating economy of the system is ensured.

The said means for cooling may include, if required, moreover a second heat exchanger or other cooling device for the cooling of the prepared fluid to consuming temperature. It is preferred though, to use this second heat exchanger or cooling device so as to bring the temperature down to a value just below the consuming temperature, and it is combined in such a case with a, preferably controllable, heating device for reheating the prepared fluid to the consuming temperature. The advantage of this design is that it is often simpler to control heating rather than cooling.

To obtain suitable temperatures in combination with a suitable sterilizing time for the water the pipeline from the said means for pumping of the water past the means for its heating and cooling respectively and up to a pressure reducing device is dimensioned so that it withstands the pressure which is required for maintaining the prepared fluid at the required sterilization temperature without the formation of steam.

A recirculation line is arranged preferably substantially between the place of consumption and the said water source. With the help of this and appropriate valves water heated to sterilizing temperature can be recirculated through the system as a whole for its sterilization.

Alternatively the sterilization can be achieved with the help of a shunt line bypassing the cold fluid side of the heat exchanger and one or more valves, with the help of which water heated to sterilizing temperature can be passed through the hot fluid side of the heat exchanger, without cooling, to succeeding parts of the system for sterilization of these parts.

The system in accordance with the invention can be used advantageously on pure water with addition at the same time of one or more concentrates in liquid and/or powder form for the preparation of a physilogically acceptable fluid, e g dialysis fluid or wound cleansing fluid, means being present for connecting up sources of these concentrates into the system between the point where the water is heated, and the point where the prepared fluid is cooled.

The said water source may be constituted of a water tank which is combined with means for the continuous returning of a part of the sterilized water to this tank. As a result the percentage impurity of the water in the tank is continuously reduced, enhancing thereby the safety of the subsequent sterilization being effective.

The said means for the returning of a part of the sterilized water to the tank may be constituted advantageously of a recirculation line which also comprises a heating device for heating the water to sterilizing temperature.

The said recirculation line preferably may form the primary side of a first heat exchanger which is dimensioned so that the water which passes through its secondary side is heated to the sterilization temperature at which it is to be maintained during the preparation of the said fluid.

Means are provided appropriately for dividing the water stream during the preparation of the said fluid into a main stream and in at least one partial stream, which is adapted to have the concentrate added to it before it is returned to the main stream, a conductivity meter being arranged in the main stream after the point of reunification with the respective partial stream. Alternatively, depending on the type of fluid that is being prepared, other measuring devices may be used, e g pH-meters or ion-selective electrodes for the checking of the solution prepared.

In a practical embodiment of the system in accordance with the invention the said water source is constituted of a water tank, from which a recirculation line originates with means for heating of the water to sterilizing temperature, before it is returned, and a line with means for the preparation of a physiologically acceptable fluid, e g dialysis fluid, a first and a second heat exchanger being arranged so that the water for the preparation of the said flud is heated first in the first heat exchanger to be cooled subsequently, after the preparation, in the second heat exchanger, whilst the water in the recirculation circuit is heated first in the second heat exchanger to be cooled, after further heating, in the first heat exchanger.

BRIEF DESCRIPTION OF DRAWINGS

Fig 1 shows a preferred embodiment of the system in accordance with the invention.

Fig 2 shows a simplified variant of the system in accordance with the invention.

Fig 3 shows a system in accordance with the invention, in which a sterile salt solution is prepared simultaneously with a sterilization of the initial fluid used.

Fig 4, finally, shows an alternative system in accordance with the invention for the preparation of a sterile salt solution simultaneously with a sterilization of the initial fluid used.

PREFERRED EMBODIMENTS OF THE SYSTEM ACCORDING TO THE INVENTION

Fig 1 shows a preferred embodiment of the system in accordance with the invention. It is an advantage of this system that the pump 8 used does not have to be heat-resistant. Nevertheless substantial parts of the system can be sterilized with the help of fluid heated to sterilization temperature within the system.

A fluid, e g water or a salt solution, of suitable chemical and microbiological quality is fed into the system at point A. With the help of the pump 8 the pressure is raised and the liquid is pumped further via a shut-off valve 1 into a heat exchanger 2 and further to a heating device, e g an electric water heater 3. The valves 9 and 11 are closed at the time. Reference 4 designates a safety valve and 5 a venting device. The outlets of these components are marked C and D and should be connected to atmosphere outside the room where the system is used, e g a hospital room. The fluid thereafter once more passes the heat exchanger 2. This time on the secondary side. The solution is cooled-via a second heat exchanger 6 to an appropriate temperature. The water for cooling is taken in at E and out at F. Tap water is generally a suitable cooling medium. The appropriate pressure of the fluid at the consuming station G is obtained by means of a pressure reducing valve 7. At the point B a facility is provided for bypassing the heat exchanger 2 via a shunt line 32, if the valve 1 is closed and the valves 9 and 11 are opened, at the same time as the valve 10 is kept closed. The latter valve is used only for emptying the system.

The invention is based on the principle that the sojourn time after heating to sterilizing temperature is at least the same as that applicable to conventional steam autoclaving of packed sterile solutions. The term sojourn time here refers to the time it takes for the solution to pass the zone heated to sterilizing temperature between the points X and Y. On passage of the solution through the secondary side of the heat exchanger 2 a part of the heat is taken up in return by the solution which passes through the primary side on the way to the sterilizing zone. In the heat exchanger 6 the temperature then is lowered further to suit the region of utilization. In the case of dialysis this can be e g 37° C.

For the sterilization of the system a facility has been installed at point B for bypassing the primary side of the heat exchanger 2. This makes it necessary that the valves 1 and 10 to be closed and the valves 9 and 11 to be kept open. When the fluid is heated to sterilizing temperature at point X this temperature is maintained through passage of the secondary side of the heat exchanger 2. The sterilizing temperature is also maintained when the solution passes the heat exchanger 6. This can be done by not allowing any cooling water to pass the primary side of this heat exchanger. Sterilization is achieved when the sojourn time between the point X and the point G, at correct temperature, is the same as that applicable to conventional steam autoclaving. This applies to the fluid. To ensure that the components after the heat excahnger 2 likewise are sterilized, these components too, of course, have to be kept heated for a corresponding period.

On heating of e g a dialysis solution some air will be liberated. This can be removed at point C. This should not be driven to the point, though, where the patient looses oxygen from the blood passing through the dialyser.

The booster pump 8 should be dimensioned so that the fluid, when it has been heated above its boiling point never passes into the steam phase, ie if the sterilization temperature is 120° C, the pump should provide a pressure which is greater than the steam pressure of the solution at 120°.

In fig 2 is shown a simplified embodiment of the system according to the invention. Here too the fluid is introduced at A, but now via a valve 12 and a pump 8'. This pump differs from the pump 8 in that it ought to be heat-resistant. The fluid thereafter is led through the heat exchanger 2 and the heating device 3 which forms the starting point X of the sterilization zone which terminates in point Y. Reference 4 designates a safety valve. If required the system may also be provided with a venting device 5 like the system according to fig 1. No such device, however, is shown in fig 2. The fluid thereafter passes the secondary side of the heat exchanger 2 and is conducted further to a heat exchanger 6 with the inlet E and the outlet F respectively. Here the fluid is cooled down appropriately to a temperature slightly below the utilization temperature to be heated subsequently to this temperature with the help of a heating device 31.

The fluid is then conducted via a controllable pressure reducing valve 7 to a shut-off valve 13, e

g a draw-off tap or some other connection.

The sterilization zone, which starts at point X, normally terminates at point Y, but can be extended in that the valves 12 and 13 are closed and the fluid is recirculated through a recirulation line 14. in this manner the pump 8′ and the components after the heat exchanger 2, including the seondary side of the latter also can be sterilized with the help of fluid heated to sterilization temperature within the system. If the valve 13 too is to be sterilized, the hot liquid can be drawn off through it during a period sufficiently long for sterility to be assured.

In fig 3 is shown a further embodiment of the system according to the invention where the water is sterilized at the same time as a dialysis solution, for example, is being prepared. In this embodiment the fluid, now water, is supplied at point A, but this time to a water tank 15. With the help of a pump 8 it is then led to a heat exchanger 2 where it is heated to sterilizing temperature. The water stream is divided thereafter into a main stream 16 and at least one partial stream 17, in the case shown here into two partial streams 17 and 18. These are controlled with the help of control valves 19 and 20. To the partial stream 17 is added a salt, e g sodium bicarbonate, if a dialysis solution is to be prepared. To this end the partial stream 17 is made to pass a column 21 which contains this salt in powder form. The addition is checked subsequently, with the help of a conductivity meter 22, which appropriately is adapted so as to control the valve 19. In the same manner a second concentrate 23 may be added to the partial stream 18 with the help of a pump 24 and be checked with the help of a conductivity meter 25 which appropriately controls the control valve 20. The addition of the two concentrates can take place essentially in the manner as described in detail, for example in the US patent 4 784 495. The prepared solution is then led to a second heat exchanger 6 and via a pressure reducing valve 7 to the consuming point G.

From the tank 15 a second partial stream 26 with the help of a pump 27 is led to the heat exchanger 6 and further to a heating device 3 throuh a line 33. The heating device 3 and the heat exchanger 2 are dimensioned 50 that a sufficiently high sterilization temperature is obtained between the points X and Y during a sufficently long time whilst the liqid passes from point X to point Y. The latter time is a function of the dimensioning of the lines for the partial streams 16, 17 and 18 and the valves and other components included therein. This applies on the assumption that the concentrate used is sterile. Otherwise the point X is shifted to point X′ with the result that the sterilization now has to be carried out between the points X′ sand Y. Reference 28 designates a three-way valve, with the help of which the fluid can be conducted either to a drain 29 or to the point of consumption G or via the line 30 back to the tank 15. The latter line is used if the system as a whole has to be sterilized, which can be done either thermally or by chemical means. The line 30 may also be used for emptying the vessel 15 to the drain 29. Reference 34, finally, designates an extra cooling device, should such a device be required at the flow and temperatures used. Alternatively 34 may designate an extra heating device if the temperature in the fluid had been reduced below the consuming temperature on passing through the heat exchanger 6.

In fig 4 is shown a further embodiment of the system in accordance with the invention where the water is sterilized at the same time as a dialysis solution, for example, is being prepared from it. In this embodiment too the water is supplied at point A to a water tank 15. The water is then conducted with the help of a pump 8 via pressure control valve 35 to the heat exchanger 2. After a preheating in the heat exchanger 2 the water is taken to a heating device 3 which is situated in a main stream 16′ corresponding to the main stream 16 in the system according to fig 3. Similarly the partial streams 17′ and 18′ with the valves 19 and 20, concentrate containers 21 and 23 and the pump 24 correspond to the partial streams 17 and 18 in fig 3 and the components provided in those streams. The flows and the concentrations in the partial streams 17′ and 18′ can be regulated with the help of the valves 19 and 20, if these are controlled by suitably placed conductivity meters (not shown) or other suitable checking devices. This check is facilitated if the two partial streams 17′ and 18′ are not joined together before reunification with the main stream 16′ because it it easier to carry out the check in the more diluted main stream in the way as illustrated in fig 3 with the help of the conductivity meters 22 and 25.

After the addition of concentrates from the partial streams 17′ and 18′ the main stream 16′ is taken via a safetly valve 4 to the secondary side of the heat exchanger 2. The sterilization takes place between the points X and Y if it is assumed that the concentrates used are sterile. Otherwise the sterilization takes place mainly between the points X′ and Y. The liquid prepared is conducted subsequently via the heat exchanger 6 and a pressure reducing valve 7 to the point of consumption G. Cooling is carried out with the help of water from the tank 15 which with the help of the pump 27 is led through the heat exchanger 6 to be returned subsequently to the tank 15. If required, an additional cooling or heating may take place in a temperature regulating device 34.

Naturally, the invention is not limited simply to the embodiments described above, but may be

varied within the scope of the following claims. Thus, for example, the components included may be varied within wide limits with regard to their form as well as to their function.

Claims

1. A method for the preparation of a sterile dialysis fluid for medical use or a similar physiologically acceptable sterile fluid by which method water is continuously transported from a source (A) for the same to a point of consumption (G), necessary concentrates in liquid and/or powder form being added during the transport, **characterized** in that the water with or without concentrate is heated during the transport to sterilizing temperature and is kept at this temperature during the time required for the sterilization, whereafter it is cooled to the desired consuming temperature.

2. A method in accordance with claim 1, **characterized** in that the cooling, at least partially, takes place by means of heat exchange with incoming, not yet heated, water.

3. A method in accordance with claim 1 or 2, **characterized** in that said concentrates in liquid and/or powder form are added simultaneously with the sterilization.

4. A method in accordance with claim 1 or 2, **characterized** in that said concentrates are added in a sterile condition.

5. A system for the preparation of a sterile dialysis fluid or a similar physiologically acceptable fluid by means of the method in accordance with anyone of the claims 1-4, comprising a pipeline between the said source for the water (A) and the point of consumption (G), e g a draw-off point, this pipeline comprising means (8,8′) for the pumping of the water, means (3) for its heating, means (2,6) for its cooling and means (eg 21 and 23) for the supply of necessary concentrates in liquid and/or powder form, **characterized** in that the pipeline between the said means (3 and 2,6) for heating and cooling respectively of the water is dimensioned so in relation to the capacity of the said means (8,8′ and 3) for pumping and heating respectively that the sojourn time of the water within this part (X-Y) of the pipeline will be sufficient for the sterilization.

6. A system in accordance with claim 5, **characterized** in that the said means for cooling comprises a heat exchanger (2) for a first cooling of the fluid with the help of incoming, not yet heated, fluid.

7. A system in accordance with claim 6, **characterized** in that the said means for cooling comprises a second heat exchanger (6) or other cooling device for the cooling of the prepared fluid to consuming temperature.

8. A system in accordance with claim 6, **characterized** in that the said means for cooling comprises a second heat exchanger (6) or other cooling device for cooling of the water to a temperature below the consuming temperature in combination with a preferably controllable heating device (31) for the heating of the prepared fluid to consuming temperature.

9. A system in accordance with claim 5, **characterized** in that the pipeline from the said means for pumping (8,8′) of the water past the means (3 and 2,6) for heating and cooling respectively of the same and up to a pressure reducing device (7) are dimensioned to withstand the pressures which are required for keeping the prepared fluid at the required sterilization temperature without the formation of steam.

10. A system in accordance with anyone of claims 5-9, **characterized** by a recirculation line (14) arranged substantially between the point of consumption (G) and the said water source (A), with the help of which water heated to sterilization temperature can be recirculated through the system as a whole for its sterilization.

11. A system in accordance with claim 6, **characterized** by a shunt line (32) leading past the cold fluid side of the heat exchanger (2) and one or more valves (1,9,11), with the help of which water heated to sterilizing temperature can be conducted through the hot fluid side of the heat exchanger (2), without cooling, to succeeding parts of the system for sterilization of these parts.

12. A system in accordance with anyone of claims 5-11, **characterized** by means for the connecting up of sources for said concentrates into the system between the point (X) where the fluid is heated, and the point (Y) where the fluid is cooled.

13. A system in accordance with anyone of claims 5-12, **characterized** in that the said water source is constituted of a water tank (15), and that means (27) are provided for the continuous returning of a part of the sterilized water to this tank.

14. A system in accordance with claim 13, **characterized** in that the said means for returning of a part of the sterilized water to the tank is constituted of a recirculation line (26, 33) which also contains a heating device (3) for the heating of the water to sterilizing temperature.

15. A system in accordance with claim 14, **characterized** in that the said recirculation line (33) forms the primary side for a first heat exchanger (2) which is dimensioned so that the water which is led through its secondary side for its part too, is heated to sterilizing temperature, and is kept at this temperature during the preparation of the said fluid.

16. A system in accordance with claim 15, **characterized** by means for dividing the water stream during the preparation of the said fluid into a main

stream (16) and at least one partial stream (17 and/or 18), which is adapted to have concentrate added to it before it is returned to the main stream, a conductivity meter (22,25) being arranged in the main stream after the point of reunification with the respective partial stream.

17. A system in accordance with claim 5, **characterized** in that the said source for the water is constituted of a water tank (15), from which starts out a recirculation line (26,33) with means (3) for the heating of the water to sterilizing temperature before it is returned, and a line (16) with means for the preparation of a physiologically acceptable fluid, e g dialysis fluid, a first (2) and a second (6) heat exchanger being arranged so that the water for the preparation of the said fluid is heated first in the first heat exchanger (2) to be cooled subsequently, after the preparation, in the second heat exchanger (6) whilst the water in the recirculation circuit is heated first in the second heat exchanger (6) to be cooled subsequently, after further heating, in the first heat exchanger (2).

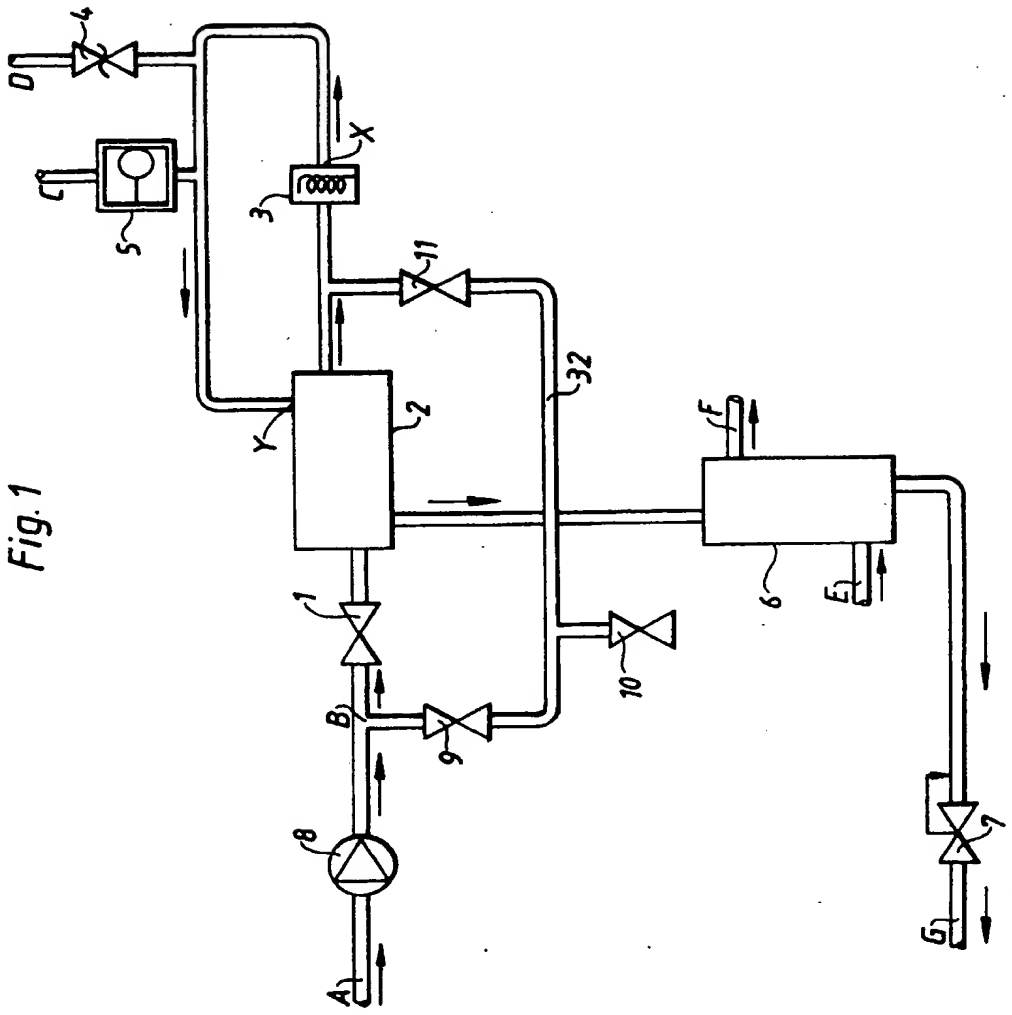
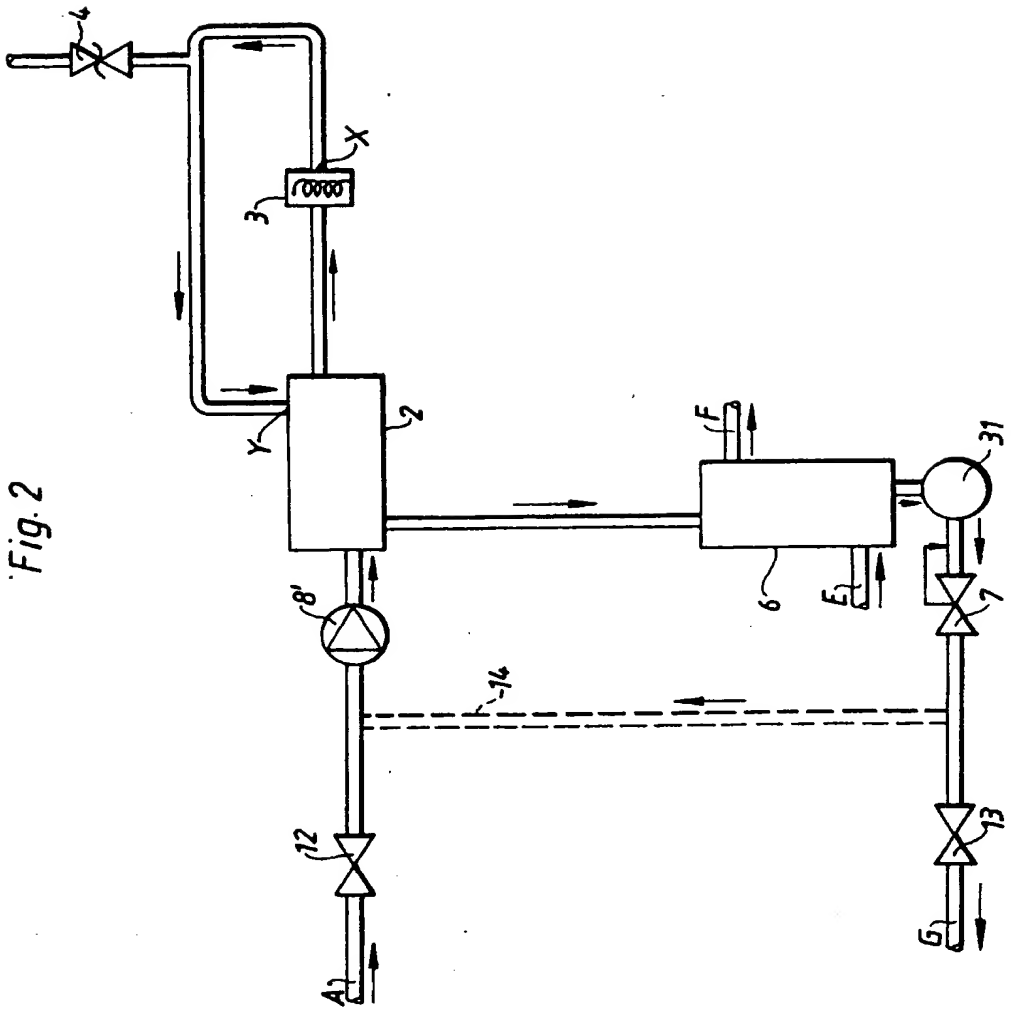


Fig. 1

Fig. 2



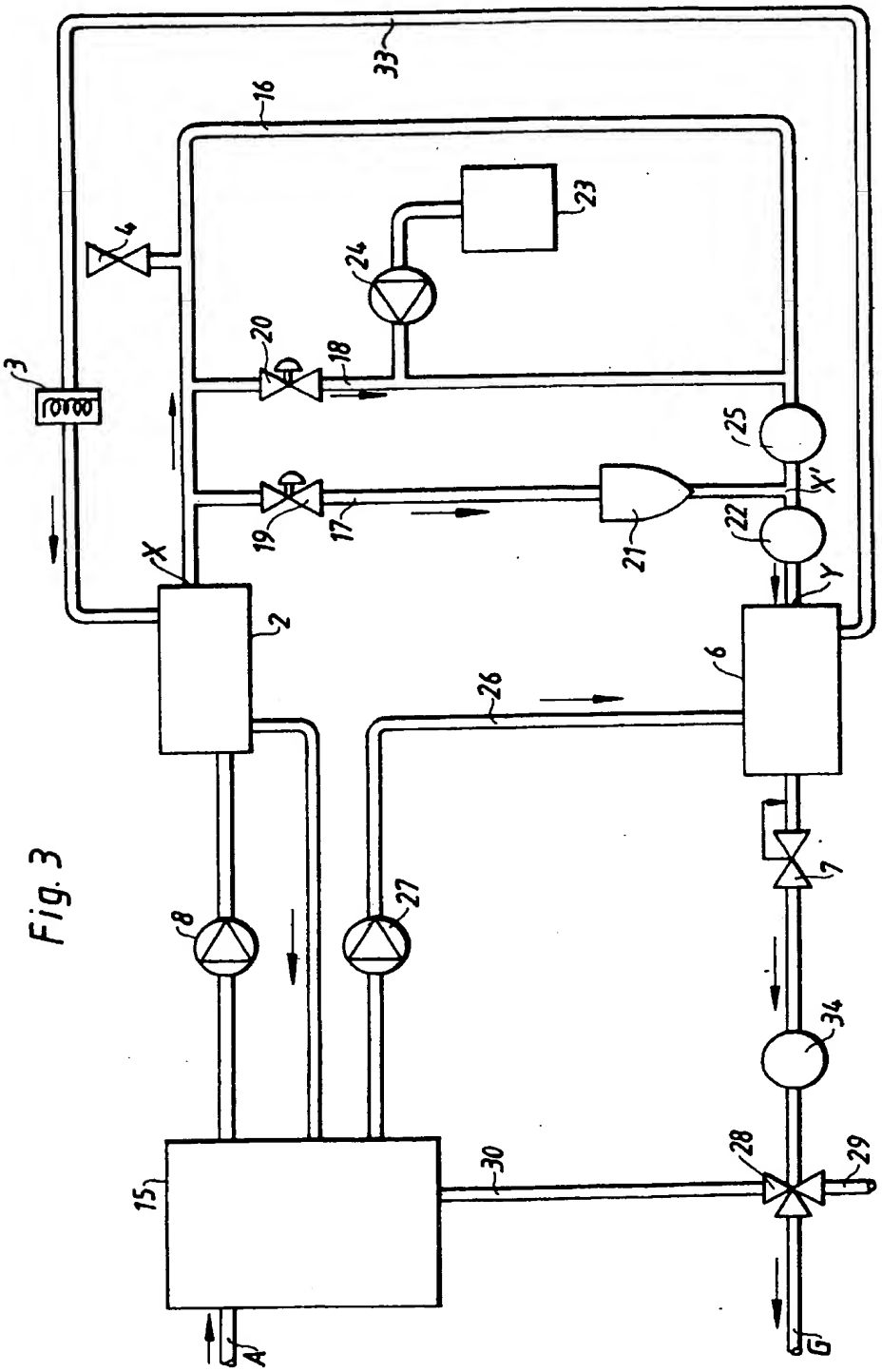


Fig. 3

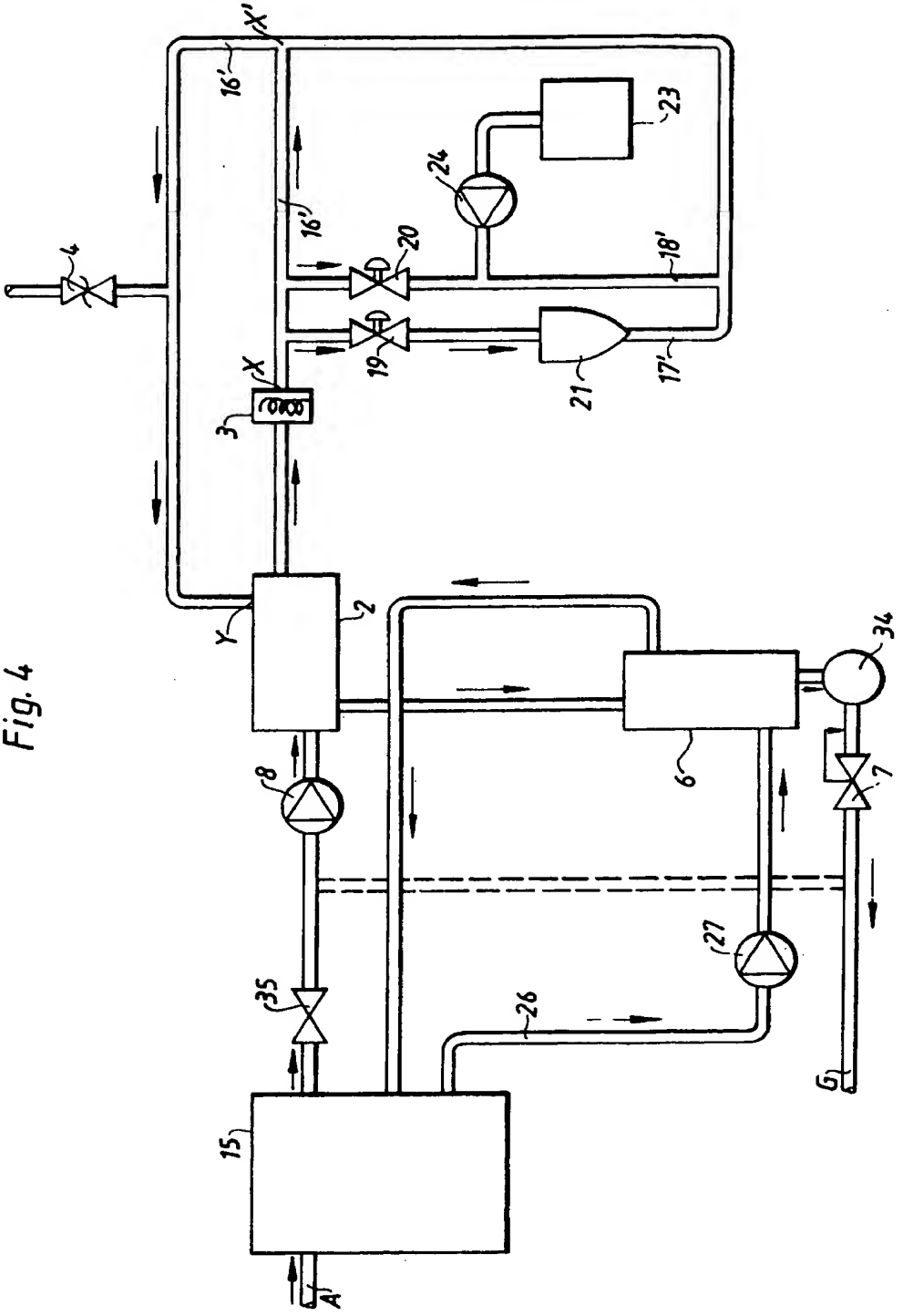


Fig. 4

European Patent Office

EUROPEAN SEARCH REPORT

Application Number

EP 90 12 0851

DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (Int. Cl.5)
X	GB-A-1 504 334 (INGERTHORPE HOLDINGS) * Page 2, line 97 - page 3, line 26; figure 1 *	1,2,4-7,9	A 61 M 1/14 A 61 L 2/04
A	FR-A-2 073 337 (NICOTRON) * Page 2, lines 15-18,30-36; page 3, lines 23-27; figure 1 *	3,12	
A	FR-A-2 627 479 (EQUIPTECHNIC) * Abstract; figure 1 *	1	

TECHNICAL FIELDS SEARCHED (Int. Cl.5)

A 61 L
A 61 M

The present search report has been drawn up for all claims

Place of search	Date of completion of the search	Examiner
THE HAGUE	29-01-1991	PAPONE F.

CATEGORY OF CITED DOCUMENTS

X : particularly relevant if taken alone
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